November 29, 2018

[Submitted electronically via www.USP.org]
United States Pharmacopeia
12601 Twinbrook Pkwy
Rockville, MD 20852

RE: Proposed Revision to General Chapter <797>

ASHP is pleased to submit comments regarding the proposed revisions to USP General Chapter <797>. ASHP represents pharmacists who serve as patient care providers in acute and ambulatory settings. The organization's 45,000 members include pharmacists, student pharmacists, and pharmacy technicians. For more than 75 years, ASHP has been at the forefront of efforts to improve medication use and enhance patient safety. ASHP has a long history of supporting the safe practice of nonsterile and sterile compounded preparations.

ASHP commends the work of the Compounding Expert Committee and USP Staff in revising General Chapter <797> and offers the following feedback on behalf of its members:

Line(s)	Comments or recommendations
8-12	Please clarify the meaning of the phrase "single patient". Does this mean one CSP for one patient; multiple CSPs for one patient (e.g. simultaneously preparing three doses of a medication given every four hours); or preparing multiple doses simultaneously for multiple patients if each preparation is for one patient?
21-23	The wording in this sentence implies that off-label preparation of CSPs is not allowed. This must be changed as the labeling of many older medications do not undergo timely updates. It also does not allow flexibility when managing drug shortages. During the shortage of small-volume saline bags, many medications were prepared differently than in product labeling in order to continue providing care for patients.
24-28	Is there any limit to the number or type of components that can be prepared for immediate administration? Is bedside TPN preparation considered acceptable? ASHP asks USP and the Expert Committee to consider circumstances like lipid formulations or preparations that require excess manipulations when establishing parameters for immediate-use preparations.
37-42	The proposed revisions do not adequately address "3) variability from the intended strength of correct ingredients." More emphasis should be placed on final product checking or verification to ensure CSPs are prepared correctly based on the formulation records. One current method of verification, known as the "syringe pullback method", has been identified by the Institute for Safe Medication Practices as a dangerous practice that can allow errors to be missed. The ASHP Council on Pharmacy Practice recently recommended a policy statement addressing the practice that will be considered by our House of Delegates for adoption. The policy statement recommends the use of automation and technology (barcode ingredient verification, image capture, gravimetric

	verification, etc.) for verifying CSP accuracy. The policy statement also discourages the use of the syringe pullback method of CSP verification. ASHP would like to see USP and the Expert Committee address the accuracy of CSP preparation in Chapter <797>.
71-77	Recommend adding ambulatory surgery centers to the list of examples as these are locations that also commonly prepare CSPs.
89-100	Recommend subheadings for "immediate use" and "future activation" to clearly delineate these requirements.
94-95	Is "attaching" the same as "docking"? If so, recommend changing language so that it's consistent.
96-99	The statement that docking proprietary bag-and-vial systems is compounding is in conflict with USP's definition of compounding since the docking of the system may be per manufacturer labeling. Even if the docking is for future use, it may still be for a specific patient. Recommend referring to this as a CSP instead of defining it as compounding.
Table 1	The establishment of Category 1 and Category 2 CSPs should simplify BUD criteria. However, ASHP is extremely concerned about the impact of the reduced BUDs for CSPs prepared in a CAI/CACI located within an SCA. In small, rural, and critical access hospitals, a full cleanroom suite is not realistic, and the use of CAI/CACIs has been an acceptable alternative. The 2017 ASHP national survey of pharmacy practice in hospital settings found that only 43% of hospitals provide 24/7 services. By limiting the BUD of CSPs prepared in a SCA with a CAI/CACI, the Expert Committee is likely increasing the amount of immediate-use compounding that will occur. This is the exact opposite intent of establishing standards for quality and safety of CSPs. ASHP strongly urges USP and the Expert Committee to consider the ramifications of limiting the BUDs of these CSPs. 1. Schneider PJ, Pedersen CA, Scheckelhoff DJ. ASHP national survey of pharmacy practice in hospital settings: dispensing and administration—2017. Am J Health-Syst Pharm. 2018; 75:1203-26.
197-199	The every-six-month visual observation of garbing and hand hygiene competency is inconsistent with the every-twelve-month requalification requirements established in Section 2.
204-207	Do the three separate gloved fingertip samples need to be consecutive? Or is it acceptable to pass one, fail several, pass another, fail several more, and then pass a third?
Table 2	ASHP recommends adding guidance as to what action should be taken if an Action Level threshold is exceeded.
Box 2.1	Recommend that all tests, whether gloved fingertip or media fill, allow a statement "or per manufacturer instructions". This would cover manufacturers that may not require warmed incubation or may not recommend inversion of plates or slides.
231-236	The inclusion of batch size in compounding conditions may not be realistic. For example, if a site frequently prepares 50 bags of vancomycin from five 10 gm vials of a pharmacy bulk package, then

	each technician who may participate in that batching process throughout their qualification period would have to prepare 50 bags of soybean-casein digest media. This would be challenging both financially and in correct incubation. Recommend setting some limit to this parameter.
247-249	Recommend providing examples of "other visual manifestations of growth": precipitate, gas bubbles, flocculence, floating debris.
285	How long is requalification good for if not compounding? For example, if a technician has not compounded for eight months, but passed requalification three months ago, they technically cannot compound. Or do the media-fill and other requalification activities count as compounding in this instance?
300-303	What guidance or criteria is a designated person expected to use to evaluate whether someone with a cold, sunburn, or conjunctivitis supposed to use to determine of the individual should be compounding? Recommend more guidance in this statement.
312	Please further define personal outer garments. Does this include religious head coverings, or can they be covered by garb? Does this require the use of facility-owned and laundered scrubs, or can compounders use scrubs that they wore to the facility?
317-318	If jewelry cannot be removed, is it acceptable to cover it with garb, or should medical tape be used?
339-342	If sterile gloves are donned prior to entering the buffer room or SCA, it might be helpful to add a reminder that they must be sterilized with IPA before compounding.
339-342	This statement implies that only sterile gloves can be worn into the cleanroom. This should not always be required if the cleanroom is being entered for purposes other than compounding (e.g. moving materials, cleaning, etc.). Please clarify this statement to specify when sterile gloves are required vs. when nonsterile gloves are appropriate.
350-352	Donning and doffing garb should be allowed by different individuals at the same time provided they do not come into contact with each other. Please add clarity or rationale to this requirement.
372-375	The word "throughout" implies continuously. Consider changing to "regularly" or "intermittently"
386-389	This statement should not apply to SCAs since they do not have to "achieve and maintain the required air quality classifications".
775-781	The Controlled Environmental Testing Association (CETA) has standards for Compounding Isolator Testing (CAG-002-2006) that assess whether the interior of the cabinet is truly isolated. If this testing is not sufficient to allow full BUDs in CAI/CACI placed in an SCA, then the chapter should include a reference or rationale to explain the decision to limit BUDs when placed in an SCA.
Box 5.2	In bullet one: is "clean" the appropriate term for sterile IPA? If the surface needs to be cleaned, a cleaning agent should be used, not a disinfectant.

Box 5.3	Similar to comments on Box 2.1, manufacturer instructions should also be considered for plating and incubating samples.
Table 8	If compounding 24 hours a day, is it really necessary to clean hoods before and after each shift? For example, the outgoing technician may clean the hood at 14:30 at the end of their shift, while the incoming technician may then clean the same hood at 15:15 at the start of their shift. Recommend adding "or every 8 hours if continuously in use" to this requirement.
1408-1409	The requirement of a MFR should be limited to batching of non-patient-specific CSPs. Patient-specific CSPs are typically compounded according to a label generated from the information technology system (electronic health record or other pharmacy system). The labels contain the ingredients needed and the amounts that will constitute the CSP. The MFR should only be required when patient labels are not available.
1410-1413	Many MFRs are part of an EHR, which is maintained by informatics specialist, not the designated person. These changes may be updated in response to regular Pharmacy and Therapeutic Committee changes, or under more time-sensitive circumstances (i.e. management of drug shortages). We recommend this be changed to state that changes to MFRs must be made according to facility SOPs which will allow more flexibility and responsiveness to facility needs.
1432-1437	As stated earlier lines in response to lines 37-42, the chapter does not adequately address final product verification checking. More emphasis should be placed on final product checking or verification to ensure CSPs are prepared correctly based on the formulation records. One current method of verification, known as the "syringe pullback method", has been identified by the Institute for Safe Medication Practices as a dangerous practice that can allow errors to be missed. The ASHP Council on Pharmacy Practice recently recommended a policy statement addressing the practice that will be considered by our House of Delegates for adoption. The policy statement recommends the use of automation and technology (barcode ingredient verification, image capture, gravimetric verification, etc.) for verifying CSP accuracy. The policy statement also discourages the use of the syringe pullback method of CSP verification. ASHP would like to see USP and the Expert Committee address the accuracy of CSP preparation in Chapter <797>.
1568-1569	Recommend adding "original" in front of "container".
1585	See previous comments on the placement of CAIs/CACIs in SCAs. Regardless of these parameters under consideration for establishing BUDs, USP and the Expert Committee have clearly put an emphasis on the environment in which the CSP is prepared regardless of the use of correct aseptic technique, storage conditions, and other factors.
1602-1604	The current Chapter <797> allows the use of "reliable literature sources and other documentation" in establishing BUD assignments. (Responsibility of Compounding Personnel section, #11; Determining Beyond-Use Dates, paragraphs 1 and 2). The absence of referring to appropriate literature sources to establish BUDs in the current chapter revision is concerning and will restrict compounders to FDA-approved labeling, only. As stated in the comments on lines 21-23,

	manufacturer labeling is often outdated and does not contain the latest information available in scientific and peer-reviewed literature. ASHP asks that USP and the Expert Committee consider adding language into the revision that specifically allows the use of appropriate literature sources when establishing BUDs.
1707-1719	Adding the definition of a single-dose container ("designed for use with a single patient as a single injection/infusion") opens the door for regulators and accreditors to restrict their use to single use regardless of the information later in the same paragraph. Recommend removing the definition and keeping the remaining language in this paragraph to make it absolutely clear that a single-dose vial can be used for up to 6 hours after initial puncture in an ISO 5 regardless of the number of patients that may have CSPs made from that vial.
1707-1719	ASHP requests that USP address the practice of drug vial optimization (DVO): the practice of using a closed-system transfer device to extend the duration a single-dose container may be used without microbial contamination. In 2018, the ASHP House of Delegates and Board of Directors approved a policy statement encouraging more research and requesting standards be developed to address DVO. <u>ASHP Policy Statement 1813: Use of Closed-System Transfer Devices to Reduce Drug Waste</u> To recognize that a growing body of evidence supports the ability of specific closed-system transfer devices (CSTDs) to maintain sterility beyond the in-use time currently recommended by United States Pharmacopeia Chapter 797, when those CSTDs are used with aseptic technique and following current sterile compounding standards; further, To foster additional research on and develop standards and best practices for use of CSTDs for drug vial optimization; further, To educate healthcare professionals, especially pharmacists and pharmacy technicians, about standards and best practices for use of CSTDs in drug vial optimization.
1716-1719	ASHP strongly supports the concept of removing vials from the ISO 5 environment after initial puncture and still allowing 6 hours of use. This will reduce the risk of error associated with having multiple vials open in the hood, as well as ensure proper airflow is maintained in the hood. We recommend adding "even if removed from the ISO 5 environment" to the end of this sentence to make it absolutely clear that the vial can be removed from the ISO 5 hood and stored elsewhere during the 6-hour interval.

General comments:

- There are many instances in the chapter where the same (or similar) information appears more than once, sometimes with inconsistencies. For example: lines 758-764 describes the process of moving materials between areas and mentions the use of gloves. However, section 6.4 also describes the cleaning and disinfecting of supplies as they move into classified spaces, and does not mention gloves.

ASHP highly recommends that the chapter be thoroughly reviewed for similar redundancies and eliminate them when possible to reduce confusion or potential conflicts in interpretation

ASHP appreciates this opportunity to provide USP with feedback on the proposed revisions to General Chapter <797>. We look forward to continuing to work with USP and the Compounding Expert Committee to protect patient and healthcare worker health and safety. Please contact me if you have any questions on ASHP's comments. I can be reached by telephone at 301-664-8617 or by email at mganio@ashp.org.

Sincerely,

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